

What is claimed is:

✓ 1. A method of analyzing a subset of nucleic acids within a nucleic acid population, comprising:

Sub A1) (a) providing a population of nucleic acid fragments at least some of which have sequences that are repeated more than once in a genome;

(b) incubating single stranded forms of the population of nucleic acid fragments under annealing conditions, whereby single stranded forms of nucleic acid fragments having repeat sequences preferentially hybridize to each other relative to nucleic acid fragments lacking repeat sequences;

(c) separating single stranded forms of the population of nucleic acid fragments from annealed double stranded forms, the single stranded forms being enriched for nucleic acid fragments lacking repeat sequence;

(d) hybridizing the separated single stranded forms of the population of nucleic acid fragments to a nucleic acid probe array,

(e) determining hybridization of the probes to the single stranded forms of the population of nucleic acid fragments, thereby analyzing the fragments.

2. The method of claim 1, wherein the population of nucleic acid fragments are genomic fragments.

3. The method of claim 1, wherein the population of nucleic acid fragments are from the human genome.

4. The method of claim 1, wherein the population of nucleic acids are from the same chromosome of the human genome.

5. The method of claim 4, wherein the population of nucleic acid fragments span the chromosome of the human genome.

6. The method of claim 1, further comprising denaturing the population of nucleic acids fragments before the incubating step.

7. The method of claim 1, wherein the separating step is performed by column chromatography.

8. The method of claim 7, wherein the column is a hydroxyapatite column.

9. The method of claim 8, wherein the separating step is performed under conditions whereby annealed and single stranded fragments elute in different fractions from the column.

10. The method of claim 1, wherein the separating step is performed by HPLC.

11. The method of claim 1, wherein the separating step is performed by successively performing hydroxyapatite chromatography and HPLC.

12. The method of claim 1, wherein the probe array comprises a set of probes complementary to a known reference sequence, the reference sequence being the same or a variant of the sequence of a nucleic acid from which the population of nucleic acid fragments was obtained.

Sub A2 > 13. The method of claim 12, wherein the determining indicates the presence of at least one variation in a fragment hybridized to the array relative to the reference sequence.

14. The method of claim 12, wherein the population of nucleic acids are from a chromosome from a first individual, and the reference sequences is that of a corresponding chromosome from a second individual.

✓ 15. A method of analyzing a subset of nucleic acids within a nucleic acid population, comprising:

- (a) providing driver and tester populations of nucleic acids;
- (b) hybridizing the driver and tester populations with each other;
- (c) separating nucleic acids from the tester population that hybridize to the driver population from tester nucleic acids that do not hybridize;
- (d) hybridizing either the tester nucleic acids that do hybridize to the driver population, or the tester nucleic acids that do not hybridize to the driver population to a nucleic acid probe array;
- (e) determining hybridization of the probes to the tester nucleic acids thereby analyzing the tester nucleic acids.

Sub A2 16. The method of claim 15, wherein the driver population of nucleic acids each bear a tag by which the driver population of nucleic acids can be immobilized to a binding moiety with affinity for the tag.

17. The method of claim 16, wherein the tag is biotin, and the binding moiety is avidin or streptavidin.

Sub A3 18. The method of claim 17, wherein the separating step is performed by immobilizing the driver population of nucleic acids and tester population of nucleic acids hybridized to the driver population via the tags of the driver population.

19. The method of claim 15, wherein the driver population of nucleic acids are a population of genomic DNA fragments, and the tester nucleic acids are a population of mRNA or nucleic acids derived therefrom, and the method further comprises denaturing tester nucleic acids from the driver population of nucleic acids after step (b), the resulting tester nucleic acids showing reduced variance in copy number between different fragments than in the population of mRNA or nucleic acids derived therefrom; and wherein the resulting tester nucleic acids are hybridized to the array.

20. The method of claim 15, wherein the driver population of nucleic acids are genomic DNA from a first source, and the tester population of nucleic acids are genomic DNA from a second source, and the method further comprises denaturing nucleic acids of the tester population from the driver population of nucleic acids after step (b), the resulting tester nucleic acids being enriched for tester nucleic acids having common sequences with the driver population of nucleic acids relative to the population of tester nucleic acids, and wherein the resulting tester nucleic acids are hybridized to the array.

21. The method of claim 20, wherein the tester population of nucleic acids are from a genome, and the driver population of nucleic acids are from at least one region of the genome, or a variant thereof from the same species as the genome.

22. The method of claim 21, wherein the at least one region is a PCR amplification product.

23. The method of claim 21, wherein the at least one region is cloned into a BAC, YAC or PAC.

24. The method of claim 21, wherein the driver population of nucleic acids are from a plurality of noncontiguous regions of the genome or the variant thereof.

25. The method of claim 21, wherein the driver population of nucleic acids are from at least ten noncontiguous regions of the genome or the variant thereof.

26. The method of claim 21, wherein the method is repeated for a further population of tester nucleic acids from a further source.

27. The method of claim 21, wherein the method is repeated for at least ten further populations of tester nucleic acids from at least ten further sources.

28. The method of claim 27, wherein the at least ten further sources are from ten individuals in the same species.

29. The method of claim 28, wherein the species is human.

30. The method of claim 15, wherein the driver population of nucleic acids are genomic DNA from a first source, and the tester population of nucleic acids are genomic DNA from a second source, and the tester nucleic acids that do not hybridize to the driver fragments are hybridized to the array, these tester nucleic acids being enriched for nucleic acids having sequences not common with sequences of the nucleic acids in the driver population.

31. The method of claim 15, wherein the driver population of nucleic acids are mRNA or nucleic acids derived therefrom, and the tester population of nucleic acids are genomic DNA; and the method further comprises denaturing tester nucleic acids from the driver population after step (b), the resulting tester nucleic acids being enriched for genomic sequences that hybridize to the mRNA; and wherein the resulting tester nucleic acids are hybridized to the nucleic acid probe array.

32. The method of claim 15, wherein the population of driver nucleic acids are mRNA or nucleic acids derived therefrom from a first source, and the population of tester nucleic acids are mRNA or nucleic acids derived therefrom from a second source, and the method further comprises denaturing tester nucleic acids from the driver nucleic acids after step (b), the resulting tester nucleic acids being enriched for nucleic acids common to the two sources, and wherein the resulting tester nucleic acids are hybridized to the nucleic acid probe array.

33. The method of claim 32, wherein the first and second source are from the same tissue of different species.

34. The method of claim 32, wherein the first and second source are from different tissues of the same species.

Sub A4 35. The method of claim 15, wherein the population of driver nucleic acids are mRNA or nucleic acids derived therefrom from a first source, and the population of tester nucleic acids are mRNA or nucleic acids derived therefrom from a second sources, the tester nucleic acids that do not hybridize with the driver nucleic acids are hybridized to the array, these tester nucleic acids s being enriched for sequence present in the second source and absent in the first source.

36. The method of claim 35, wherein the first and second source are from the same tissue of different species.

37. The method of claim 35, wherein the first and second source are from different tissues of the same species.